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Search Results -

Term	Documents
OCULAR.DWPI,EPAB,JPAB,USPT.	17370
OCULARS.DWPI,EPAB,JPAB,USPT.	403
HYPERTENSION.DWPI,EPAB,JPAB,USPT.	26015
HYPERTENSIONS.DWPI,EPAB,JPAB,USPT.	120
(2 AND (OCULAR ADJ HYPERTENSION)).USPT,JPAB,EPAB,DWPI.	16

Database:

US Patents Full-Text Database
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EPO Abstracts Database
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IBM Technical Disclosure Bulletins

l2 and ocular hypertension

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Search History

Today's Date: 9/30/2000

DB Name	Query	Hit Count	Set Name
USPT,JPAB,EPAB,DWPI	l2 and ocular hypertension	16	L5
USPT,JPAB,EPAB,DWPI	grbeta or gr-beta	1	L4
USPT,JPAB,EPAB,DWPI	l2 and glucocorticoid receptor beta	0	L3
USPT,JPAB,EPAB,DWPI	l1 and glucocorticoid receptor	66	L2
USPT,JPAB,EPAB,DWPI	glaucoma	7491	L1

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Search Results - Record(s) 1 through 1 of 1 returned.

1. Document ID: WO 9824932 A1

L4: Entry 1 of 1   File: EPAB   Jun 11, 1998

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PUB-NO: WO009824932A1
DOCUMENT-IDENTIFIER: WO 9824932 A1
TITLE: METHODS FOR DIAGNOSING GLAUCOMA AND DISCOVERING
ANTI-GLAUCOMA DRUGS
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Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image

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Term	Documents
GRBETA.DWPI,EPAB,JPAB,USPT.	1
GRBETAS	0
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GR-BETAS	0
(GR-BETA OR GRBETA).USPT,JPAB,EPAB,DWPI.	1

| Display | 20 | Documents, starting with Document: | 1 |

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L5: Entry 9 of 16   File: USPT   Dec 29, 1998

DOCUMENT-IDENTIFIER: US 5854415 A
TITLE: Methods for the diagnosis of glaucoma

ABPL:
A glucocorticoid-induced protein, TIGR, that is produced by
cells of the trabeclar meshwork can be used to diagnose
glaucoma. The TIGR protein, anti-TIGR antibodies, and TIGR
encoding sequences also provide a diagnostic for glaucoma and
its related diseases.

GOPR:
The present invention is in the fields of diagnostics, and
concerns methods and reagents for diagnosing glaucoma and
related disorders. This invention was supported with Government
funds (NIH EY02477 and NIH EY 08905-02). The Government has
certain rights in this invention.

BSPR:
"Glaucomas" are a group of debilitating eye diseases that are
the leading cause of preventable blindness in the United States
and other developed nations. Primary Open Angle Glaucoma
("POAG") is the most common form of glaucoma. The disease is
characterized by the degeneration of the trabecular meshwork,
leading to obstruction of the normal ability of aqueous humor
to leave the eye without closure of the space (e.g., the
"angle") between the iris and cornea (see, Vaughn, D. et al.,
In: General Ophthamology, Appleton & Lange, Norwalk, Conn., pp.
213-230 (1992)). A characteristic of such obstruction in this
disease is an increased intraocular pressure ("IOP"), resulting
in progressive visual loss and blindness if not treated
appropriately and in a timely fashion.

BSPR:
A link between the IOP response of patients to glucocorticoids
and the disease of POAG has long been suspected. While only 5%
of the normal population shows a high IOP increase (16 mm Hg)
to topical glucocorticoid testing, over 90% of patients with
POAG show this response. In addition, an open angle glaucoma
may be induced by exposure to glucocorticoids. This observation
has suggested that an increased or abnormal glucocorticoid
response in trabecular cells may be involved in POAG (Zhan, G.
L. et al., Exper. Eye Res. 54:211-218 (1992); Yun, A. J. et
al., Invest. Ophthamol. Vis. Sci. 30:2012-2022 (1989); Clark,
A. F., Exper. Eye Res. 55:265 (1992); Klemetti, A., Acta
Ophthamol. 68:29-33 (1990); Knepper, P. A., U.S. Pat. No.
4,617,299).

BSPR:
The ability of glucocorticoids to induce a glaucoma-like
condition has led to efforts to identify genes or gene products
that would be induced by the cells of the trabecular meshwork
in response to glucocorticoids (Polansky, J. R. et al., In:
Glaucoma Update IV, Springer-Verlag, Berlin pp. 20-29 (1991)).
Initial efforts using short-term exposure to dexamethasone
revealed only changes in specific protein synthesis. Extended
exposure to relatively high levels of dexamethasone was,
however, found to induce the expression of related 66 kD and 55
kD proteins that could be visualized by gel electrophoresis
(Polansky, J. R., et al., In: Glaucoma Update IV,
Springer-Verlag, Berlin, pp. 20-29 (1991)). The induction
kinetics of these proteins as well as their dose response
characteristics were similar to the kinetics those that were
required for steroid-induced IOP elevation in human subjects
(Polansky, J. R. et al., In: Glaucoma Update IV,
Springer-Verlag, Berlin, pp. 20-29 (1991)). Problems of
aggregation and apparent instability or loss of protein in the
purification process were obstacles in obtaining a direct
protein sequence.

BSPR:
Because increased IOP is a readily measurable characteristic of
glaucoma, the diagnosis of the disease is largely screened for
by measuring intraocular pressure (tonometry) (Strong, N. P.,
Ophthal, Physiol. Opt. 12:3-7 (1992), Greve, M. et al., Can. J.
Ophthamol. 28:201-206 (1993)). Unfortunately, because
glaucomatous and normal pressure ranges overlap, such methods
are of limited value unless multiple readings are obtained
(Hitchings, R. A., Br. J. Ophthamol. 77:326 (1993); Tuck, M. W.
et al., Ophthal. Physiol. Opt. 13:227-232 (1993); Vaughan, D.
et al., In: General Ophthamology, Appleton & Lange, Norwalk,
Conn. pp. 213-230 (1992); Vernon, S. A., Eye 7:134-137 (1993)).
For this reason, additional methods, such as direct examination
of the optic disk and determination of the extent of a
patient's visual field loss are often conducted to improve the
accuracy of diagnosis (Greve, M. et al., Can. J. Ophthamol.
28:201-206 (1993)).

BSPR:
In view of the importance of glaucoma, and the at least partial
inadequacies of prior methods of diagnosis, it would be
desirable to have an improved, more accurate method for
diagnosing glaucoma. The present invention provides such
improved diagnostic agents and methods.

BSPR:
The invention concerns a novel peptide sequence discovered to
be highly induced by glucocorticoids in the endothelial lining
cells of the human trabecular meshwork. The cDNA for this
protein, the protein itself, molecules that bind to it, and
nucleic acid molecules that encode it, provide improved methods
and reagents for diagnosing glaucoma and related disorders, as
well as for diagnosing other diseases or conditions, such as
cardiovacsular, immunological, or other diseases or conditions

that affect the expression or activity of the protein. Indeed,
the molecules of the present invention may be used to diagnose
diseases or conditions which are characterized by alterations
in the expression of extracellular proteins. In addition, due
to its cellular functions and DNA binding properties, the
molecules of the present invention may be used to diagnose
diseases or conditions which are characterized those functions.

BSPR:
The invention also provides a method for diagnosing glaucoma in
a patient which comprises determining whether the amount of a
TIGR protein present in the trabecular meshwork of an eye of
the patient exceeds the amount of that TIGR protein present in
the trabecular meshwork of an eye of an individual who is not
suffering from glaucoma, wherein the detection of an excessive
amount of the TIGR protein is indicative of glaucoma.

BSPR:
The invention also provides a method for quantitatively or
qualitatively determining the amount of a TIGR protein present
in the trabecular meshwork of an eye of an individual, and
determining whether that amount exceeds the amount of that TIGR
protein present in the trabecular meshwork of an eye of an
individual who is not suffering from glaucoma, wherein the
detection of an excessive amount of the TIGR protein is
indicative of glaucoma.

DEPR:
As indicated above, the trabecular meshwork has been proposed
to play an important role in the normal flow of the aqueous,
and has been presumed to be the major site of outflow
resistance in glaucomatous eyes. Human trabecular meshwork
(HTM) cells are endothelial like cells which line the outflow
channels by which aqueous humor exits the eye; altered
synthetic function of the cells may involve in the pathogenesis
of steroid glaucoma and other types of glaucoma. Sustained
steroid treatment of these cells are interesting because it
showed major difference was observed when compared to 1-2 day
glucocorticoid (GC) exposure, which appears relevant to the
clinical onset of steroid glaucoma (1-6 weeks).

DEPR:
Despite decades of research, prior to the present invention,
the molecular basis for glaucoma had not been determined
(Snyder, R. W. et al., Exper. Eye Res. 57:461-468 (1993);
Wiggs, J. L. et al., Genomics 21:299-303 (1994)).

DEPR:
The II.2 clone is 2.0 Kb whereas the Northern blotting shows a
band of 2.5 Kb. Although not including a poly A tail, the 3'
end of the clone contains two consensus polyadenylation
signals. Southern analysis suggested two groups of genomic
sequences and two genomic clones were isolated. In-situ
hybridization using these genomic probes shows that the TIGR
gene and/or a sequence or sequences that specifically hybridize
to the TIGR gene are located on chromosome 1, p36 and 10.11 or

12, p13, p15. Further in-situ hybridization using the P.sub.1 TIGR clone (P.sub.1 TIGR DNA was deposited on May 14, 1996, American Type Culture Collection, 12301 Parklawn Drive, Rockville, Md. 20852, USA) shows an additional TIGR gene and/or a sequence or sequences that specifically hybridize to the TIGR gene located at chromosome 1, q20-26, and most preferably at chromosome 1, q23-24. Clone P.sub.1 TIGR comprises human genomic sequences that specifically hybridize to the TIGR gene cloned into the BamHI site of vector pCYPAC (Ioannou et al., Nature Genetics, 6:84-89 (1994) herein incorporated by reference). Study of cyclohexamide treatment in the absence and presence of GC suggest that the induction of TIGR may involve factors in addition to the GC receptor. The TIGR gene may be involved in the cellular stress response since it is also induced by stimulants such as H.sub.2 O.sub.2, TPA, glucose and heat; this fact may relate to glaucoma pathogenesis and treatment.

DEPR:
The TIGR protein also contains 5 putative O-linked glycosylation sites throughout the molecule. "Leucine zipper" regions define a helical structure that permits protein-protein binding to occur (see, generally, Tso, J. Y. et al., PCT Patent Application WO93/11162; Land, K. H. et al., PCT Patent Application WO/93/191761). The TIGR protein contain 7 leucine zipper units. The presence of the zipper regions provides a means for the TIGR molecules to bind to one another forming macromolecular and possible aggregation. Studies showing the binding of this molecule to HTM cells (but not to fibroblast cells) support the notion that is can influence the outflow pathway in HTM tissue to cause the increased intra-ocular pressure that characterizes glaucoma and its related diseases. TIGR protein has also been successfully expressed using the baculovirus system and Sf9 insect cells. The major recombinant proteins are the two 55 kd cellular proteins encoded by the TIGR cDNA. Antibodies produced from these protein recognize both the cellular 55 kD proteins and the secreted 66 kD glycosylated form of these proteins in dexamethasome-treated HTM cells and in organ culture systems. In situ analysis of glaucomatous tissue specimens show a high expression level of this protein relative to normal controls.

DEPR:
The presence, induction, and level of the TIGR secretory protein mirror the onset and kinetics with which glucocorticoids induce glaucoma, and the glucocorticoid-induced expression of this secretory protein comprises the molecular basis for glaucoma and its related diseases. Such an understanding of the molecular basis permits the definition of diagnostic agents for glaucoma and its related diseases.

DEPR:
As used herein, the term "glaucoma" has its art recognized meaning, and includes both primary glaucomas, secondary glaucomas, and familial (i.e. inherited glaucomas). The methods of the present invention are particularly relevant to the diagnosis of POAG, OAG, juvenile glaucoma, and inherited

glaucomas. A disease or condition is said to be related to
glaucoma if it possesses or exhibits a symptom of glaucoma, for
example, an increased intra-ocular pressure resulting from
aqueous outflow resistance (see, Vaughan, D. et al., In:
General Ophthamology, Appleton & Lange, Norwalk, Conn., pp.
213-230 (1992)). The preferred agents of the present invention
are discussed in detail below.

DEPR:
The agents of the present invention are capable of being used
to diagnose the presence or severity of glaucoma and its
related diseases in a patient suffering from glaucoma (a
"glaucomatous patient"). Such agents may be either naturally
occurring or non-naturally occurring. As used herein, a
naturally occurring molecule may be "substantially purified,"
if desired, such that one or more molecules that is or may be
present in a naturally occurring preparation, containing that
molecule will have been removed or will be present at a lower
concentration than that at which it would normally be found.

DEPR:
In one embodiment, such nucleic acid molecules will encode all
or a fragment of TIGR protein, its "promoter" or flanking gene
sequences. As used herein, the term "promoter" is used in an
expansive sense to refer to the regulatory sequence(s) that
control mRNA production. Such sequences include RNA polymerase
binding sites, glucocorticoid response elements, enhancers,
etc. All such TIGR molecules may be used to diagnose the
presence of glaucoma and severity of glaucoma.

DEPR:
One aspect of the present invention concerns antibodies,
single-chain antigen binding molecules, or other proteins that
specifically bind to TIGR protein and its analogs, fusions or
fragments. Such antibodies are "anti-TIGR antibodies," and may
be used to diagnose glaucoma and its related diseases. As used
herein, an antibody or peptide is said to "specifically bind"
to TIGR if such binding is not competitively inhibited by the
presence of non-TIGR molecules.

DEPR:
Nucleic acid molecules that encode all or part of the TIGR
protein can be expressed, via recombinant means, to yield TIGR
protein or peptides that can in turn be used to elicit
antibodies that are capable of binding TIGR. Such antibodies
may be used in immunodiagnostic assays of glaucoma. Such
TIGR-encoding molecules, or their fragments may be a "fusion"
molecule (i.e. a part of a larger nucleic acid molecule) such
that, upon expression, a fusion protein is produced.

DEPR:
The ability to produced antibodies that bind TIGR molecules
permits the identification of mimetic compounds of TIGR. A
"mimetic compound" of TIGR is a compound that is not TIGR, or a
fragment of TIGR, but which nonetheless exhibits an ability to
specifically find to anti-TIGR antibodies. Such molecules can
be used to elicit anti-TIGR antibodies, and thus, may be used

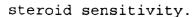to assist the diagnosis of glaucoma and its related diseases.

DEPR:
A particularly desired use of the present invention relates to
the diagnosis of glaucoma, POAG, pigmentary glaucoma, high
tension glaucoma and low tension glaucoma and their related
diseases. As used herein the term "glaucoma" refers to
glaucoma, POAG, pigmentary glaucoma, and low tension glaucoma
and their related diseases. As indicated above, methods for
diagnosing glaucoma suffer from inaccuracy, or require multiple
examinations. The molecules of the present invention may be
used to define superior assays for glaucoma. Quite apart from
such usage, the molecules of the present invention may be used
to diagnosis or protect an individual's sensitivity to elevated
intraocular pressure upon administration of steroids such as
glucocorticoids or corticosteroids). Dexamethasone, cortisol
and prednisolone are preferred steroids for this purpose.
Medical conditions such as inflammatory and allergic disorders,
as well as organ transplantation recipients, benefit from
treatment with glucocorticoids. Certain individuals exhibit an
increased sensitivity to such steroids (i.e., "steroid
sensitivity"), which is manifested by an undesired increase in
intraocular pressure. The present invention may be employed to
diagnosis or predict such sensitivity, as well as glaucoma and
related diseases.

DEPR:
In a first embodiment, the TIGR molecules of the present
invention are used to determine whether an individual has a
mutation affecting the level (i.e., the concentration of TIGR
mRNA or protein in a sample, etc.) or pattern (i.e., the
kinetics of expression, rate of decomposition, stability
profile, etc.) of the TIGR expression (collectively, the "TIGR
Response" of a cell or bodily fluid) (for example, a mutation
in the TIGR gene, or in a regulatory region(s) or other gene(s)
that control or affect the expression of TIGR), and being
predictive of individuals who would be predisposed to glaucoma,
related diseases, or steroid sensitivity. As used herein, the
TIGR Response manifested by a cell or bodily fluid is said to
be "altered" if it differs from the TIGR Response of cells or
of bodily fluids of normal individuals. Such alteration may be
manifested by either abnormally increased or abnormally
diminished TIGR Response. To determine whether a TIGR Response
is altered, the TIGR Response manifested by the cell or bodily
fluid of the patient is compared with that of a similar cell
sample (or bodily fluid sample) of normal individuals. As will
be appreciated, it is not necessary to re-determine the TIGR
Response of the cell sample (or bodily fluid sample) of normal
individuals each time such a comparison is made; rather, the
TIGR Response of a particular individual may be compared with
previously obtained values of normal individuals.

DEPR:
In one sub-embodiment, such an analysis is conducted by
determining the presence and/or identity of polymorphism(s) in
the TIGR gene or its flanking regions which are associated with
glaucoma, or a predisposition to glaucoma, related diseases, or

steroid sensitivity.

DEPR:
Other known nucleic acid amplification procedures, such as
allele-specific oligomers, branched DNA technology,
transcription-based amplification systems, or isothermal
amplification methods may also be mused to amplify and analyze
such polymorphisms (Malek, L. T. et al., U.S. Pat. No.
5,130,238; Davey, C. et al., European Patent Application
329,822; Schuster et al., U.S. Pat. No. 5,169,766; Miller, H.
I. et al., PCT appln. WO 89/06700; Kwoh, D. et al., Proc. Natl.
Acad. Sci. (U.S.A.) 86:1173 (1989); Gingeras, T. R. et al., PCT
application WO 88/10315; Walker, G. T. et al., Proc. Natl.
Acad. Sci. (U.S.A.) 89:392-396 (1992)). All the foregoing
nucleic acid amplification methods coupled be used to predict
or diagnose glaucoma.

DEPR:
The identification of a polymorphism in the TIGR gene can be
determined in a variety of ways. By correlating the presence or
absence of glaucoma in an individual with the presence or
absence of a polymorphism in the TIGR gene or its flanking
regions, it is possible to diagnose the predisposition of an
asymptomatic patient to glaucoma, related diseases, or steroid
sensitivity. If a polymorphism creates or destroys a
restriction endonuclease cleavage site, or if it results in the
loss or insertion of DNA (e.g., a VNTR polymorphism), it will
alter the size or profile of the DNA fragments that are
generated by digestion with that restriction endonuclease. As
such, individuals that possess a variant sequence can be
distinguished from those having the original sequence by
restriction fragment analysis. Polymorphisms that can be
determined in this manner are termed "restriction fragment
length polymorphisms" ("RFLPs"). RFLPs have been widely used in
human and animal genetic analyses (Glassberg, J., UK patent
Application 2135774; Skolnick, M. H. et al., Cytogen. Cell
GEnet. 32:58-67 (1982); Botstein, D. et al., Ann. J. Hum.
Genet. 32:314-331 (1980); Fischer, S. G et al. (PCT Application
WO90/13668); Uhlen, M., PCT Application WO90/11369)). The role
of TIGR in glaucoma pathogenesis indicates that the presence of
genetic alterations (e.g., DNA polymorphisms) that affect the
TIGR Response can be employed to predict glaucoma.

DEPR:
In accordance with this embodiment of the invention, a sample
DNA is obtained from a patient's cells. In a preferred
embodiment, the DNA sample is obtained from the patient's
blood. However, any source of DNA may be used. The DNA is
subjected to restriction endonuclease digestion. TIGR is used
as a probe in accordance with the above-described RFLP methods.
By comparing the RFLP pattern of the TIGR gene obtained from
normal and glaucomatous patients, one can determine a patient's
predisposition to glaucoma. The polymorphism obtained in this
approach can then be cloned to identify the mutation at the
coding region which alters the protein's structure or
regulatory region of the gene which affects its expression
level. Changes involving promoter interactions with other

regulator proteins can be identified by, for example, gel shift assays using HTM cell extracts, fluid from the anterior chamber of the eye, serum, etc. Interactions of TIGR protein in glaucomatous cell extracts, fluid from the anterior chamber of the eye, serum, etc. can be compared to control samples to thereby identify changes in those properties of TIGR that relate to the pathogenesis of glaucoma. Similarly such extracts and fluids as well as others (blood, etc.) can be used to diagnosis or predict steroid sensitivity.

DEPR:
In a second embodiment, the previously described "anti-TIGR antibodies" are employed in an immunodiagnostic assay for glaucoma and its related diseases.

DEPR:
As discussed above, TIGR protein is secreted extracellularly from the trabecular meshwork into the extracellular matrix of the trabecular meshwork, and thus may pass out into the body fluids. This characteristic permits one to assay TIGR concentrations in blood, lymph, or serum, and to thereby determine whether a patient's TIGR levels exceed those found in the blood of individuals who do not have glaucoma and are not predisposed to glaucoma related diseases or steroid sensitivity. Patients found to have altered levels of TIGR thus may be diagnosed as glaucoma.

DEPR:
Thus, a third aspect of the present invention concerns the recognition that one can diagnosis or predict glaucoma related diseases or steroid sensitivity by determining the TIGR Response of cells or tissue other than the trabecular meshwork.

DEPR:
In one sub-embodiment of this aspect of the present invention, one can diagnose or predict glaucoma related diseases and steroid sensitivity by ascertaining the TIGR Response in a biopsy (or a macrophage or other blood cell sample), or other cell sample, or more preferably, in a sample of bodily fluid (especially, blood, serum, plasma, tears, etc.). Since the TIGR gene is induced in response to the presence of glucocorticoids, a highly preferred embodiment of this method comprises ascertaining such TIGR Response prior to, during and/or subsequent to, the administration of a glucocorticoid. Thus, by way of illustration, glaucoma could be diagnosed or predicted by determining whether the administration of a glucocorticoid (administered topically, intraocularly, intramuscularly, systemically, or otherwise) alters the TIGR Response of a particular individual, relative to that of normal individuals. Most preferably, for this purpose, at least a "TIGR gene-inducing amount" of the glucocorticoid will be provided. As used herein, a TIGR gene-inducing amount of a glucocorticoid is an amount of glucocorticoid sufficient to cause a detectable indication of TIGR expression in cells of glaucomatous or non-glaucomatous individuals.

DEPR:
In an alternative diagnostic format, ocular tissue (obtained,
for example by trabeculotomy) may be evaluated in an in situ
immunodiagnostic assay for glaucoma and its related diseases.

DEPR:
In such a format, antibodies (especially labeled antibodies) or
other TIGR-binding peptide are incubated in the presence of
ocular tissue in order to evaluate the clinical degree and
significance of glaucoma in biopsied tissue. The extent,
location, or degree of TIGR in the ocular tissue is determined
by staining or other visualization methods. Such information is
then compared to the staining pattern obtained from normal or
glaucomatous individuals in order to diagnose or predict
glaucoma.

DEPR:
As discussed above, TIGR protein exhibits an ability to
self-aggregate, due at least in part to the presence of leucine
zippers in the molecule. Because small peptide fragments of
TIGR that possess such zipper regions can bind to TIGR, such
peptides may be used as alternatives to anti-TIGR antibodies in
diagnostic assays. The use of such peptides is desirable since
the peptides can be modified to possess both lipophilic and
hydrophilic groups. The presence of such groups will permit the
peptide to traverse the corneal membrane. Thus, such agents may
be provided topically in an eye drop or ointment, and can be
used in the same manner as anti-TIGR antibodies to effect the
diagnosis of glaucoma. The peptide will desirably be labeled
with a fluorescent group to facilitate detection.

DEPR:
Northern analysis showed clone TIGR to be approximately 2.5 kb,
and to encode a protein of unique sequence. The induction of
the mRNA required protein synthesis and insulin-like growth
factor reduced the induction effect by 50%. The TIGR mRNA
indication was not observed in dexamethasone treated
fibroblasts, keratinocytes, or ciliary epithelial cells. The
pattern of induction in HTM cells was distinguishable from
other steroid induced proteins such as metallothionine,
alpha.sub.1 -acid glycoprotein, and TAT which were maximally
induced by one day dexamethasone treatment. In addition to
dexamethasone, the TIGR mRNA was induced in HTM cells exposed
to hydrogen peroxide, TPA, or glucose for 3-24 hours.
Dexamethasone treatment produced substantial loss in the mRNAs
for glucocorticoid receptors and heat shock proteins (e.g., hsp
90 mRNA levels fell approximately 20 fold after 10 days of
dexamethasone treatment).

DEPC:
III. Uses of the Molecules of the Invention in the Diagnosis of
Glaucoma and Related Diseases

ORPL:
Stone et al., "Identification of a Gene that Causes Primary
Open Angle Glaucoma", Science 275:668-670 (1997).

ORPL:
Clark, A.F., "Evaluation of Anti-Glaucoma Compounds and
Discovery of Pathogenic Mechanisms using Perfusion Cultured
Human Eyes," Exper. Eye Res. 55Ab266 (1992).

ORPL:
Zhan, G.L., et al., Steroid Glaucoma: Corticosteroid-Induced
Ocular Hypertension in Cats, Exper. Eye Res. 54:211-218 (1992).

ORPL:
Nguyen, T.D. et al., "Molecular Biology Studies of
Steroid-Induced Glaucoma Model Using Cultured Human Trabecular
Meshwork," Invest Ophthalmol Vis. Sci. 32789 (1991).

ORPL:
Polansky, J.R., et al., "In Vitro Correlates of Glucocorticoid
Effects on Intraocular Pressure," In: Glaucoma Update IV,
Springer-Verlag, Berlin, pp. 20-29 (1991).

ORPL:
Weinreb, R.N., et al., "Detection of Glucocorticoid Receptors
in Cultured Human Trabecular Cells," Invest Ophthalmol. Vis.
Sci. 21:403-407 (1981).

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L5: Entry 10 of 16   File: USPT   Aug 4, 1998

US-PAT-NO: 5789169
DOCUMENT-IDENTIFIER: US 5789169 A

TITLE: Methods for the diagnosis of glaucoma

DATE-ISSUED: August 4, 1998

INVENTOR-INFORMATION:
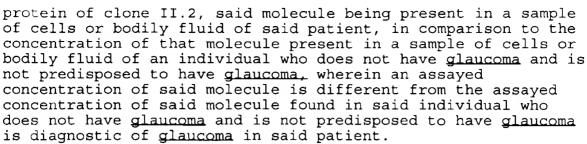| NAME	CITY	STATE	ZIP CODE	COUNTRY
Nguyen; Thai D.	Mill Valley	CA	N/A	N/A
Polansky; Jon R.	Mill Valley	CA	N/A	N/A
Huang; Weidong	Irvine	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/7.1, 435/91.2

CLAIMS:

What is claimed is:
1. A method for diagnosing glaucoma in a patient which
comprises determining whether the amount of the secretory
protein encoded by clone II.2 present in the trabecular
meshwork of an eye of said patient exceeds the amount of said
protein present in the trabecular meshwork of an eye of an
individual who does not have glaucoma and is not predisposed to
have glaucoma, wherein the detection of an altered amount of
said protein is indicative of glaucoma.
2. The method of claim 1, wherein said determination is
accomplished by determining the amount of an mRNA molecule that
encodes the secretory protein of clone II.2 present in cells of
the trabecular meshwork.
3. The method of claim 1, wherein said determination is
accomplished by administering an antibody capable of
specifically binding to the secretory protein encoded by clone
II.2 to said patient and determining the extent to which said
antibody binds to the extracellular matrix of the trabecular
meshwork.
4. The method of claim 1, wherein said determination is
accomplished by administering a peptide that binds the
secretory protein encoded by clone II.2 of said patient and
determining the extent to which said peptide binds to the
extracellular matrix of the trabecular meshwork.
5. A method for diagnosing glaucoma in a patient under
evaluation for suspected glaucoma which comprises assaying the
concentration of a molecule, whose concentration is dependent
upon the expression of a gene that encodes the secretory

protein of clone II.2, said molecule being present in a sample
of cells or bodily fluid of said patient, in comparison to the
concentration of that molecule present in a sample of cells or
bodily fluid of an individual who does not have glaucoma and is
not predisposed to have glaucoma, wherein an assayed
concentration of said molecule is different from the assayed
concentration of said molecule found in said individual who
does not have glaucoma and is not predisposed to have glaucoma
is diagnostic of glaucoma in said patient.
6. The method of claim 5, wherein said bodily fluid is selected
from the group consisting of glaucomatous cell extract, fluid
from the anterior chamber of the eye, blood, lymph and serum.
7. The method of claim 5, wherein said molecule is a protein
molecule expressed by said gene.
8. The method of claim 5, wherein said molecule is an mRNA
molecule encoded by said gene, or a cDNA molecule encoded by
said gene.
9. The method of claim 8, wherein said concentration of said
mRNA molecule is assayed by incubating a sample of said bodily
fluid in the presence of a nucleic acid molecule that
hybridizes to said mRNA molecule.
10. The method of claim 5, wherein prior to performing said
assay, said patient is provided with a gene that encodes the
secretory protein of clone II.2-inducing amount of a
glucocorticoid; and wherein said comparison is made between the
concentration of said molecule in said sample of cells or
bodily fluid of said patient, and the concentration of said
molecule in a sample of cells or bodily fluid of an individual
who does not have glaucoma and is not predisposed to have
glaucoma, but who has also received said gene-inducing amount
of a said glucocorticoid.
11. The method of claim 10, wherein said molecule is an mRNA
molecule encoded by said gene, or a cDNA molecule encoded by
said gene.
12. The method of claim 10, wherein said molecule is a protein
molecule expressed by said gene.
13. The method of claim 7, wherein said expression of said gene
is assayed by incubating a sample of said cells or said bodily
fluid in the presence of antibodies elicited in response to
immunization of an antibody-producing cell with a recombinantly
produced secretory protein encoded by clone II.2, wherein said
antibody molecule binds the secretory protein encoded by clone
II.2.
14. The method of claim 13, wherein said antibodies recognize a
protein molecule expressed by steroid-treated human trabecular
cells.
15. A method for diagnosing glaucoma in a patient which
comprises the steps:
(A) incubating under conditions permitting nucleic acid
hybridization: a marker nucleic acid molecule, said marker
nucleic acid molecule comprising a nucleotide sequence of a
polynucleotide that specifically hybridizes to a polynucleotide
that is linked to a gene that encodes the secretory protein of
clone II.2, and a complementary nucleic acid molecule obtained
from a cell or a bodily fluid of said patient, wherein nucleic
acid hybridization between said marker nucleic acid molecule,
and said complementary nucleic acid molecule obtained from said

patient permits the detection of a polymorphism whose presence
is predictive of a mutation affecting the level or pattern of
said secretory protein of clone II.2 in said patient;
(B) permitting hybridization between said marker nucleic acid
molecule and said complementary nucleic acid molecule obtained
from said patient; and
(C) detecting the presence of said polymorphism, wherein the
detection of said polymorphism is diagnostic of glaucoma.
16. The method of claim 15, wherein said level of said
secretory protein of clone II.2 is predictive.
17. The method of claim 15, wherein said pattern of said
secretory protein of clone II.2 is predictive.
18. The method of claim 15, wherein said marker nucleic acid
molecule comprises a nucleotide sequence of a polynucleotide
that is genetically linked to said gene, and has the sequence
of a polynucleotide of chromosome 1, q.
19. The method of claim 18, wherein said marker nucleic acid
molecule comprises a nucleotide sequence of a polynucleotide
that is genetically linked to said gene, and has the sequence
of a polynucleotide of chromosome 1, q21-26.
20. The method of claim 19, wherein said marker nucleic acid
molecule comprises a nucleotide sequence of a polynucleotide
that is genetically linked to said gene, and has the sequence
of a polynucleotide of chromosome 1, q23-24.
21. The method of claim 15, wherein said marker nucleic acid
molecule comprises a nucleotide sequence of a polynucleotide
that is physically linked to within 1 mb of said gene.
22. The method of claim 15, wherein said marker nucleic acid
molecule comprises a nucleotide sequence of a polynucleotide
that is physically linked to within 100 kb of said gene.
23. The method of claim 15, wherein said marker nucleic acid
molecule comprises a nucleotide sequence of a polynucleotide
that is physically linked to within 10 kb of said gene.
24. The method of claim 15, wherein said marker nucleic acid
molecule comprises a nucleic acid molecule that encodes the
secretory protein of clone II.2 or fragment thereof.
25. The method of claim 15, wherein said bodily fluid is
selected from the group consisting of glaucomatous cell
extract, fluid from the anterior chamber of the eye, blood,
lymph and serum.
26. The method of claim 15, wherein said complementary nucleic
acid molecule obtained from a cell or present in a bodily fluid
of said patient is expressed by steroid-treated cells.
27. The method of claim 27, wherein said bodily fluid is ocular
aqueous, and wherein said cells are HTM cells.
28. A method for diagnosing glaucoma in a patient which
comprises the steps:
(A) obtaining a sample of cells or bodily fluid from said
patient;
(B) determining whether said sample contains the secretory
protein encoded by clone II.2 whose presence is predictive of a
mutation affecting the level or pattern of said protein in said
patient; wherein the detection of said protein is diagnostic
for glaucoma.
29. A method for diagnosing steroid sensitivity in a patient
under evaluation for suspected steroid sensitivity which
comprises the steps:

(A) obtaining a sample of cells or bodily fluid from said patient;

(B) assaying said sample to determine the concentration of a molecule, whose concentration is dependent upon the expression of a gene that encodes the secretory protein of clone II.2, in comparison to the concentration of that molecule present in a sample of cells or bodily fluid of an individual who does not have steroid sensitivity and is not predisposed to have steroid sensitivity, wherein an assayed concentration of said molecule is different from the assayed concentration of said molecule found in said individual who does not have steroid sensitivity and is not predisposed to have steroid sensitivity is diagnostic of steroid sensitivity in said patient.

30. The method of claim 29, wherein said bodily fluid is selected from the group consisting of fluid from the anterior chamber of the eye, blood, lymph and serum.

31. The method of claim 30, wherein said molecule is an mRNA molecule encoded by said gene, or a cDNA molecule encoded by said gene.

32. The method of claim 31, wherein said concentration of said mRNA molecule is assayed by incubating a sample of said bodily fluid in the presence of a nucleic acid molecule that hybridizes to said mRNA molecule.

33. The method of claim 29, wherein said molecule is a protein molecule expressed by said gene.

34. The method of claim 30, wherein prior to performing said assay, said patient is provided with a gene that encodes the secretory protein of clone II.2-inducing amount of a glucocorticoid; and wherein said comparison is made between the concentration of said molecule in said sample of cells or bodily fluid of said patient, and the concentration of said molecule in a sample of cells or bodily fluid of an individual who does not have steroid sensitivity and is not predisposed to have steroid sensitivity, but who has also received said gene-inducing amount of a said glucocorticoid.

35. A method for diagnosing steroid sensitivity in a patient which comprises the steps:

(A) incubating under conditions permitting nucleic acid hybridization: a marker nucleic acid molecule, said marker nucleic acid molecule comprising a nucleotide sequence of a polynucleotide that specifically hybridizes to a polynucleotide that is linked to a gene that encodes the secretory protein of clone II.2, and a complementary nucleic acid molecule obtained from a cell or a bodily fluid of said patient, wherein nucleic acid hybridization between said marker nucleic acid molecule, and said complementary nucleic acid molecule obtained from said patient permits the detection of a polymorphism whose presence is predictive of a mutation affecting the level or pattern of said secretory protein of clone II.2 in said patient;

(B) permitting hybridization between said marker nucleic acid molecule and said complementary nucleic acid molecule obtained from said patient; and

(C) detecting the presence of said polymorphism, wherein the detection of said polymorphism is diagnostic of steroid sensitivity.

36. The method of claim 35, wherein said level of said secretory protein of clone II.2 is predictive.

37. The method of claim 35, wherein said pattern of said secretory protein of clone II.2 is predictive.

38. The method of claim 35, wherein said complementary nucleic acid molecule obtained from a cell or a bodily fluid of said patient has been amplified using a nucleic acid amplification method.

39. The method of claim 38, wherein said nucleic acid amplification method is polymerase chain amplification.

40. The method of claim 38, wherein said nucleic acid amplification method is ligase chain reaction.

41. The method of claim 38, wherein said nucleic acid amplification method is oligonucletide ligation assay.

42. The method of claim 35, wherein said detecting the presence of said polymorphism is by allelic specific oligomers.

43. The method of claim 35, wherein said detecting the presence of said polymorphism is by branched DNA technology.

44. The method of claim 38, wherein said nucleic acid amplification method is transcription base amplification.

45. The method of claim 38, wherein said nucleic acid amplification method is iso thermal amplification.

46. The method of claim 15, wherein said complementary nucleic acid molecule obtained from a cell or a bodily fluid of said patient has been amplified using a nucleic acid amplification method.

47. The method of claim 46, wherein said nucleic acid amplification method is polymerase chain amplification.

48. The method of claim 46, wherein said nucleic acid amplification method is ligase chain reaction.

49. The method of claim 46, wherein said nucleic acid amplification method is oligonucletide ligation assay.

50. The method of claim 15, wherein said detecting the presence of said polymorphism is by allelic specific oligomers.

51. The method of claim 15, wherein said detecting the presence of said polymorphism is by branched DNA technology.

52. The method of claim 46, wherein said nucleic acid amplification method is transcription base amplification.

53. The method of claim 46, wherein said nucleic acid amplification method is iso thermal amplification.

54. A method for diagnosing glaucoma in a patient which comprises the steps:

(A) incubating under conditions permitting nucleic acid hybridization: a marker nucleic acid molecule, said marker nucleic acid molecule comprising a nucleotide sequence of a polynucleotide that specifically hybridizes to a polynucleotide that is linked to a sequence that specifically hybridizes to a gene that encodes the secretory protein of clone II.2, and a complementary nucleic acid molecule obtained from a cell or a bodily fluid of said patient, wherein nucleic acid hybridization between said marker nucleic acid molecule, and said complementary nucleic acid molecule obtained from said patient permits the detection of a polymorphism whose presence is predictive of a mutation affecting the level or pattern of said secretory protein of clone II.2 in said patient;

(B) permitting hybridization between said marker nucleic acid molecule and said complementary nucleic acid molecule obtained from said patient; and

(C) detecting the presence of said polymorphism, wherein the

detection of said polymorphism is diagnostic of <u>glaucoma</u>.

55. The method of claim 54, wherein said level of said secretory protein of clone II.2 is predictive.

56. The method of claim 54, wherein said pattern of said secretory protein of clone II.2 is predictive.

57. The method of claim 54, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is genetically linked to a sequence that specifically hybridizes to said gene, and has the sequence of a polynucleotide of chromosome 1, q.

58. The method of claim 57, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is genetically linked to said gene, and has the sequence of a polynucleotide of chromosome 1, q21-26.

59. The method of claim 58, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is genetically linked to a sequence that specifically hybridizes to said, and has the sequence of a polynucleotide of chromosome 1, q23-24.

60. The method of claim 54, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is physically linked to within 1 mb of a sequence that specifically hybridizes to said gene.

61. The method of claim 54, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is physically linked to within 100 kb to a sequence that specifically hybridizes to said gene.

62. The method of claim 54, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is physically linked to within 10 kb to a sequence that specifically hybridizes to said gene.

63. The method of claim 54, wherein said marker nucleic acid molecule comprises a sequence that specifically hybridizes to said gene-encoding nucleic acid molecule, or fragment thereof.

64. The method of claim 54, wherein said bodily fluid is selected from the group consisting of glaucomatous cell extract, fluid from the anterior chamber of the eye, blood, lymph and serum.

65. The method of claim 54, wherein said complementary nucleic acid molecule obtained from a cell or present in a bodily fluid of said patient is expressed by steroid-treated cells.

66. The method of claim 54, wherein said bodily fluid is ocular aqueous, and wherein said cells are HTM cells.

67. A method for diagnosing <u>glaucoma</u> in a patient under evaluation for suspected <u>glaucoma</u> which comprises assaying the concentration of a molecule, whose concentration is dependent upon the expression of a gene, said gene having a nucleic acid sequence which specifically hybridizes to SEQ ID NO: 3 and which encodes for a glucocorticoid inducible 66 kD glycosylated protein and a glucocorticoid inducible 55 kD protein, said molecule being present in a sample of cells or bodily fluid of said patient, in comparison to the concentration of that molecule present in a sample of cells or bodily fluid of an individual who does not have <u>glaucoma</u> and is not predisposed to have <u>glaucoma</u>, wherein an assayed concentration of said molecule is different from the assayed concentration of said molecule in said individual who does not have <u>glaucoma</u> and is

not predisposed to have glaucoma is diagnostic of glaucoma in said patient.

68. The method of claim 67, wherein said bodily fluid is selected from the group consisting of glaucomatous cell extract, fluid from the anterior chamber of the eye, blood, lymph and serum.

69. The method of claim 67, wherein said molecule is a protein molecule expressed by said gene.

70. The method of claim 67, wherein said molecule is an mRNA molecule encoded by said gene, or a cDNA molecule encoded by said gene.

71. The method of claim 70, wherein said concentration of said mRNA molecule is assayed by incubating a sample of said bodily fluid in the presence of a nucleic acid molecule that hybridizes to said mRNA molecule.

72. The method of claim 69, wherein said expression of said gene is assayed by incubating a sample of said cells or said bodily fluid in the presence of antibodies elicited in response to immunization of an antibody-producing cell with a protein selected from the group consisting of a recombinantly produced glucocorticoid inducible 66 kD glycosylated protein, and recombinantly produced glucocorticoid inducible 55 kD protein, wherein said antibody molecule binds said recombinantly produced glucocorticoid inducible 66 kD glycosylated protein or said recombinantly produced glucocorticoid inducible 55 kD protein.

73. The method of claim 72, wherein said antibodies recognize a protein molecule expressed by steroid-treated human trabecular cells.

74. A method for diagnosing glaucoma in a patient which comprises the steps:

(A) incubating under conditions permitting nucleic acid hybridization: a marker nucleic acid molecule, said marker nucleic acid molecule comprising a nucleic acid molecule that is linked to a gene, said gene having a nucleic acid sequence which specifically hybridizes to SEQ ID NO: 3 and which encodes for a glucocorticoid inducible 66 kD glycosylated protein and a glucocorticoid inducible 55 kD protein, and a complementary nucleic acid molecule obtained from a cell or a bodily fluid of said patient, wherein nucleic acid hybridization between said marker nucleic acid molecule and said complementary nucleic acid molecule obtained from said patient permits the detection of a polymorphism whose presence is predictive of a mutation affecting the level or pattern of said glucocorticoid inducible 66 kD glycosylated protein or said glucocorticoid inducible 55 kD protein in said patient;

(B) permitting hybridization between said marker nucleic acid molecule and said complementary nucleic acid molecule obtained from said patient; and

(C) detecting the presence of said polymorphism, wherein the detection of said polymorphism is diagnostic of glaucoma.

75. The method of claim 74, wherein said level is predictive.

76. The method of claim 74, wherein said pattern is predictive.

77. The method of claim 74, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is genetically linked to said gene, and has the sequence

of a polynucleotide of chromosome 1, q.

78. The method of claim 77, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is genetically linked to said gene, and has the sequence of a polynucleotide of chromosome 1, q21-26.

79. The method of claim 78, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is genetically linked to said gene, and has the sequence of a polynucleotide of chromosome 1, q23-24.

80. The method of claim 74, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is physically linked to within 1 mb of said gene.

81. The method of claim 74, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is physically linked to within 100 kb of said gene.

82. The method of claim 74, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is physically linked to within 10 kb of said gene.

83. The method of claim 74, wherein said marker nucleic acid molecule comprises a nucleic acid sequence which specifically hybridizes to SEQ ID NO: 3 and which encodes for a glucocorticoid inducible 66 kD glycosylated protein or fragment thereof and a glucocorticoid inducible 55 kD protein or fragment thereof.

84. The method of claim 74, wherein said bodily fluid is selected from the group consisting of glaucomatous cell extract, fluid from the anterior chamber of the eye, blood, lymph and serum.

85. The method of claim 74, wherein said complementary nucleic acid molecule obtained from a cell or present in a bodily fluid of said patient is expressed by steroid-treated cells.

86. The method of claim 74, wherein said bodily fluid is ocular aqueous, and wherein said cells are HTM cells.

87. A method for diagnosing steroid sensitivity in a patient under evaluation for suspected steroid sensitivity which comprises assaying the concentration of a molecule, whose concentration is dependent upon the expression of a gene, said gene having a nucleic acid sequence which specifically hybridizes to SEQ ID NO: 3 and which encodes for a glucocorticoid inducible 66 kD glycosylated protein and a glucocorticoid inducible 55 kD protein, said molecule being present in a sample of cells or bodily fluid of said patient, in comparison to the concentration of that molecule present in a sample of cells or bodily fluid of an individual who does not have steroid sensitivity and is not predisposed to have steroid sensitivity, wherein an assayed concentration of said molecule is different from the assayed concentration of said molecule in said individual who does not have steroid sensitivity and is not predisposed to have steroid sensitivity is diagnostic of steroid sensitivity in said patient.

88. The method of claim 87, wherein said bodily fluid is selected from the group consisting of glaucomatous cell extract, fluid from the anterior chamber of the eye, blood, lymph and serum.

89. The method of claim 87, wherein said molecule is a protein molecule expressed by said gene.

90. The method of claim 87, wherein said molecule is an mRNA

molecule encoded by said gene, or a cDNA molecule encoded by said gene.

91. The method of claim 87, wherein said concentration of said mRNA molecule is assayed by incubating a sample of said bodily fluid in the presence of a nucleic acid molecule that hybridizes to said mRNA molecule.

92. The method of claim 87, wherein said expression of said gene is assayed by incubating a sample of said cells or said bodily fluid in the presence of antibodies elicited in response to immunization of an antibody-producing cell with a protein selected from the group consisting of a recombinantly produced glucocorticoid inducible 66 kD glycosylated protein, and recombinantly produced glucocorticoid inducible 55 kD protein, wherein said antibody molecule binds said recombinantly produced glucocorticoid inducible 66 kD glycosylated protein or said recombinantly produced glucocorticoid inducible 55 kD protein.

93. The method of claim 92, wherein said antibodies recognize a protein molecule expressed by steroid-treated human trabecular cells.

94. A method for diagnosing steroid sensitivity in a patient which comprises the steps:

(A) incubating under conditions permitting nucleic acid hybridization: a marker nucleic acid molecule, said marker nucleic acid molecule comprising a nucleic acid molecule that is linked to gene, said gene having a nucleic acid sequence which specifically hybridizes to SEQ ID NO: 3 and which encodes for a glucocorticoid inducible 66 kD glycosylated protein and a glucocorticoid inducible 55 kD protein, and a complementary nucleic acid molecule obtained from a cell or a bodily fluid of said patient, wherein nucleic acid hybridization between said marker nucleic acid molecule and said complementary nucleic acid molecule obtained from said patient permits the detection of a polymorphism whose presence is predictive of a mutation affecting the level or pattern of said glucocorticoid inducible 66 kD glycosylated protein or said glucocorticoid inducible 55 kD protein in said patient;

(B) permitting hybridization between said marker nucleic acid molecule and said complementary nucleic acid molecule obtained from said patient; and

(C) detecting the presence of said polymorphism, wherein the detection of said polymorphism is diagnostic of steroid sensitivity.

95. The method of claim 94, wherein said level is predictive.

96. The method of claim 94, wherein said pattern is predictive.

97. The method of claim 94, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is genetically linked to said gene, and has the sequence of a polynucleotide of chromosome 1, q.

98. The method of claim 94, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is genetically linked to said gene, and has the sequence of a polynucleotide of chromosome 1, q21-26.

99. The method of claim 94, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is genetically linked to said gene, and has the sequence

of a polynucleotide of chromosome 1, q23-24.

100. The method of claim 94, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is physically linked to within 1 mb of said gene.

101. The method of claim 94, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is physically linked to within 100 kb of said gene.

102. The method of claim 94, wherein said marker nucleic acid molecule comprises a nucleotide sequence of a polynucleotide that is physically linked to within 10 kb of said gene.

103. The method of claim 94, wherein said marker nucleic acid molecule comprises a nucleic acid sequence which specifically hybridizes to SEQ ID NO: 3 and which encodes for a glucocorticoid inducible 66 kD glycosylated protein or fragment thereof and a glucocorticoid inducible 55 kD protein or fragment thereof.

104. The method of claim 94, wherein said bodily fluid is selected from the group consisting of glaucomatous cell extract, fluid from the anterior chamber of the eye, blood, lymph and serum.

105. The method of claim 94, wherein said complementary nucleic acid molecule obtained from a cell or present in a bodily fluid of said patient is expressed by steroid-treated cells.

106. The method of claim 94, wherein said bodily fluid is ocular aqueous, and wherein said cells are HTM cells.